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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/007,093	01/14/98	ANAND	N	1038-765-MIS

HM12/0408

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EXAMINER	
TUNG, M	
ART UNIT	PAPER NUMBER
1644	5

DATE MAILED: 04/08/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/007,093	Applicant(s) Anand, et al.
	Examiner Mary Tung	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Jan 14, 1998*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11, 27, and 28* is/are pending in the application.

Of the above, claim(s) ____ is/are withdrawn from consideration.

☐ Claim(s) ____ is/are allowed.

☒ Claim(s) *1-11, 27, and 28* is/are rejected.

☐ Claim(s) ____ is/are objected to.

☐ Claims ____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on ____ is/are objected to by the Examiner.

☒ The proposed drawing correction, filed on *Jan 14, 1998* is ☐ approved ☒ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) ____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: ____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). ____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Mary Tung, Group Art Unit 1644, Group 1640, Technology Center 1600.

DETAILED ACTION

Priority

2. This application is a continuation of 08/483,576.

3. This application filed under *37 C.F.R. § 1.60* lacks the necessary reference to the prior application. A statement reading "This is a continuation of application Serial No. 08/483,576, filed June 7, 1995" should be entered following the title of the invention or as the first sentence of the specification. Also, the present status of all parent applications should be included.

Election/Restriction

4. Applicant's election of Group I claims 1-11, 27 and 28 in the paper filed January 25, 1999, Paper No. 4 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Acknowledgment is made of the cancellation, in Paper No. 4, of claims 12-25, recited in Group II.

Information Disclosure Statement

5. The applicants indicate in the paper filed 1/14/98 (Paper No. 2) that an IDS and PTO Form 1449 were being submitted. However, said form and IDS was not present in the file.

Drawings

6. The drawings are objected to because each figure must be labeled. Figures 6, 9, and 10 comprise 2 or more views, each view should be labeled separately. Figure 6 should be amended to be Figures 6A and 6B, etc. The specification and the brief description of the drawings should be amended to reflect these changes.

Abstract

7. The Abstract of the Disclosure is objected to because it is in the form of two paragraphs. The abstract should be in narrative form and generally limited to a **single paragraph** within the range of 50 to 250 words. Correction is required. See M.P.E.P. § 608.01(b).

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Specification

8. The specification needs to be amended on page 19, lines 15 and 16 to reflect the new address of the ATCC repository. The new address is: ATCC, 10801 University Boulevard, Manassas, VA 20110-2209.

9. The use of the trademarks such as "GENE AMP," p 20, line 13, "FAST TRACK," page 20, line 32, "cDNA SYNTHESIS PLUS," page 20, line 34, "cDNA CLONING SYSTEM," page 21, line 1, and so on, of the specification has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

10. Each letter of the trademarks must be capitalized. *See MPEP 608.01(V)* and *Appendix 1*.

Claim Rejections - 35 U.S.C. § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-11, 27 and 28 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 1 and 27 are indefinite because it is unclear whether the antigen presenting cells are genetically modified or whether the antibody conjugate molecule is genetically modified.

14. Claims 27 and 28 read on a compound, because no carrier is recited in the claims. Since any protein could be immunogenic or tolerogenic, applicants need to clarify which additional components would be present to affect the recited immunogenic affect. Applicants are also reminded to avoid new matter, if amending the claims.

15. Claims 1 and 27 recite the phrase "exclusively at at least one", which renders the claims indefinite. It is unclear how the claimed product could be exclusive, and more than one concurrently. Also the double article in this phrase is confusing.

16. The term "weakly" in claim 7 is a relative term which renders the claim indefinite. The term "weakly" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

17. Claims 2-11 recite the term 'molecule", which lacks an antecedent basis in base claim 1. It is suggested that the term be modified to recite "a recombinant conjugate antibody molecule".

18. Claim 8 recites the phrase "wherein said at least one antigen moiety comprises a plurality of antigen moieties." It is unclear how one could have one antigen moiety, encompassed by the phrase "at least one" and have more than one, at the same time. Clarification is required.

Claim Rejections - 35 U.S.C. § 102

19. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 1, 2, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Barber (US Patent #4,950,480).

21. The '480 patent teaches an antibody conjugate molecule specific for a surface structure of antigen presenting cells which comprises an antigen, and wherein the antigen presenting cells are class I major histocompatability complex expressing cells, or class II major histocompatability complex expressing cells, (see col. 2, lines 17-31 and col. 3, lines 12-40), and an immunogenic composition (see col. 2, lines 34-41 (vaccine composition), col 5, lines 3-6 and 37-42). The recitation of the bivalent antibody having heavy and light chains is an inherent property of antibodies, absent a teaching of antibody fragments. Additionally, the limitation that the antibody is recombinant lends no patentable weight to the claimed invention, since a product is a product, regardless of its process of manufacture. Also, the intended use recitation of delivering the antigen to antigen presenting cells, also lends no patentable weight to these product claims. Therefore, the reference teachings anticipate the claimed invention.

22. Claims 1, 2, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Barber (US Patent #5,194,254).

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23. The '254 patent teaches an antibody conjugate molecule specific for a surface structure of antigen presenting cells which comprises an antigen, and wherein the antigen presenting cells are class I major histocompatability complex expressing cells, or class II major histocompatability complex expressing cells, (see col. 2, lines 21-29 and col. 3, lines 40-56 and col. 5, lines 9-15), and an immunogenic composition (see col 3, line 64 and bridging over to col 4, line 34 and col lines 3-6 and 37-42). The recitation of the bivalent antibody having heavy and light chains is an inherent property of antibodies, absent a teaching of antibody fragments. Additionally, the limitation that the antibody is recombinant lends no patentable weight to the claimed invention, since a product is a product, regardless of its process of manufacture. Also, the intended use recitation of delivering the antigen to antigen presenting cells, also lends no patentable weight to these product claims. Therefore, the reference teachings anticipate the claimed invention.

24. Claims 1-11 and 27-28 are rejected under 35 U.S.C. § 102(a) as being anticipated by Baier et al.(U).

25. Baier et al.(U) teach a recombinant antibody conjugates recombinantly produced using chimeric genes that encode fusion proteins of antibody fragments expressing short, immunogenic HIV-1 peptides (page 2358, col. 1, paragraph 1) and wherein said antibody conjugate were specific for antigen presenting cells and was known in the art (see page 2357, col. 2 paragraph 2, page 2363, col. 1, paragraph 2 and col. 2, paragraph 2. Additionally, Baier et al. teach chimeric anti-human HLA-DR class II antigens and that HIV-derived epitopes are located at the C-terminal end of the antibody (page 2358, col. 1, paragraph 2 and page 2360, Figure 1), as recited in claims 1, 2 and 27. Furthermore, Baier et al. teach bivalent monoclonal antibodies, which inherently would have heavy and light chains, absent evidence to the contrary (see page 2363, col. 2 paragraph 2), as recited in claims 3-6. Baier et al. teach that chimeric antibodies can be used to overcome the inherently weak immunogenicity of a peptide, as recited in claim 7. Baier, et al. additionally teach that multiple similar or different, antigen moieties can be conjugated to said antibodies (see page 2358, paragraph 1), as recited in claims 8-10. An antigen having two 15 amino acids is taught on page 2359, col. 1, first paragraph under the heading of "RESULTS", as recited in claim 11. The chimeric Fabs bound specifically to human ANTIGEN PRESENTING CELLS displaying the relevant HLA-DR molecules and demonstrated improved immunogenicity as measured by increased stimulation of IL-2 production in vitro by human $CD4^+$ Th cells from donors exposed to HIV-1 antigens (page 2358, in particular), and thus, an immunogenic composition, as recited in claim 28. Therefore, the claimed inventions is anticipated by the reference teaching.

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Response to Arguments

26. Applicant's arguments filed 1/14/98 (Paper No. 2) have been fully considered but they are not persuasive.

27. The applicants argue that the '480 patent does not teach the instant invention as claimed because the "chemical coupling technique employed by Barber, et al, such as yield (typically about 20%)", variability between preparations, loss of material during purification is overcome by the instant application by adding the limitations of genetic modification and the "antigen moiety being present exclusively at at least one preselected site on the monoclonal antibody moiety." However, as stated previously, the applicant must show that the recombinant antigen-antibody fusion proteins have *properties* which differ from the chemically conjugated fusion proteins. There is no such showing in the instant application. Additionally, the limitation of exclusively at at least one preselected site encompasses antibodies which also have binding at other sites. The "exclusive binding" is limited to one (or more) preselected site, but does not also preclude binding at other sites as well, especially in light of the open "contain" language of claims 1 and 27. There is no showing that the instantly-claimed antibodies have properties that are different than taught in the '480 patent. Furthermore, there is no showing that the antibodies taught in the '480 patent do not include the antibodies as recited in the instant application. The '480 patent is silent about the structure of the antibodies taught therein, therefore, absent evidence to the contrary, there is a presumption that the antibodies are not distinct.

28. The applicants argue that the teachings of Baier, et al., do not encompass the instant invention, in that Baier utilizes monoclonal antibody Fab *fragments*, which would not read on claims 1 and 27, as amended in Paper No. 2. of the instant application. However, Baier clearly teaches bivalent monoclonal antibodies, which inherently would have heavy and light chains, absent evidence to the contrary (see page 2363, col. 2 paragraph 2), as recited in claims 3-6. Therefore, Baier, et al. (U) anticipates the claimed invention in claims 1-11, 27 and 28, as discussed, *supra.*

Claim Rejections - 35 U.S.C. § 103

29. The following is a quotation of *35 U.S.C. § 103* which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under *subsection (f) or (g)* of *section 102* of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

30. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

31. Claims 1-4, 27 and 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barber (US Patent No. 4,950,480) in view of Skea (V).

32. The '480 patent has been discussed *supra*. The claimed invention differs from the reference teaching only by the recitation of an antigen moiety being located on at least one end of the heavy and light chains, as recited in claim 3 or on the C-terminal end of at least one of the heavy or light chains of the monoclonal antibody, as recited in claim 4. However, in order to use the anti-class II major histocompatability complex monoclonal antibodies as a delivery vehicle for antigen, the two molecules were coupled with avidin as a bridge with minimal disruption to each in a method to more efficiently immune animals against the taught antigen, Skea teaches a monoclonal antibody conjugate with an antigen attached to the C-terminal end of the molecule (see Figure 2, panel (a). The recitation "located at the C-terminal end" comprises the reference molecule because there is no recitation by the applicants of which part of the C-terminal end the antigen is located. One of ordinary skill in the art at the time the invention was made would have been motivated to use the anti-class II major histocompatability complex monoclonal antibodies as a delivery vehicle for antigen, wherein the two molecules are coupled with avidin as a bridge with minimal disruption to each in a method to more efficiently immune animals against the taught antigen, using a monoclonal antibody conjugate with an antigen attached to the C-terminal end of the molecule as taught by Skea (see Figure 2, panel (a)) in the monoclonal antibody composition taught by the '480 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

33. Claims 1-4, 27 and 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barber (US Patent No. 5,194,254) in view of Skea (V).

34. The '254 patent has been discussed *supra*. The claimed invention differs from the reference teaching only by the recitation of an antigen moiety being located on at least one end of the heavy and light chains, as recited in claim 3 or on the C-terminal end of at least one of the heavy or light chains of the monoclonal antibody, as recited in claim 4. However, in order to use the anti-class II major histocompatability complex monoclonal antibodies as a delivery vehicle for antigen, the two molecules were coupled with avidin as a bridge with minimal disruption to each in a method to more efficiently immune animals against the taught antigen, Skea teaches a monoclonal antibody conjugate with an antigen attached to the C-terminal end of the molecule (see Figure 2, panel (a). The recitation "located at the C-terminal end" comprises the reference molecule because there is no recitation by the applicants of which part of the C-terminal end the antigen is located. One of ordinary skill in the art at the time the invention was made would have been motivated to use the anti-class II major histocompatability complex monoclonal antibodies as a delivery vehicle for antigen, wherein the two molecules are coupled with avidin as a bridge with minimal disruption to each in a method to more efficiently immune animals against the taught antigen, using a monoclonal antibody conjugate with an antigen attached to the C-terminal end of the molecule as taught by Skea (see Figure 2, panel (a)) in the monoclonal antibody composition taught by the '254 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

35. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

36. A timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. 1.130(b).

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37. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. 3.73(b).

38. Claims 1-11, 27 and 28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 4,950,480.

39. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conjugate antibody molecule, specific for an antigen presenting cell surface structure, which express major histocompatability complex antigens class I and II , as recited in claim 2 of the instant application, comprising an antigen, as recited in claims 1 and 27, or wherein the antigen moiety is weakly antigenic, as recited in claim 7, or wherein there is a plurality of antigen moieties, as recited in claims 8-10, or wherein said composition is formulated as a vaccine, as recited in claim 28, is not patentably distinct over the antibody conjugate recited in the '480 patent. The '480 patent recites an antibody conjugate molecule, specific for an antigen presenting cell surface structure (antigen presenting cells comprise B cells and macrophages), which express major histocompatability complex class I and II antigens, as recited in claims 2-5, comprising an antigen, as recited in claim 1, or wherein the antigen moiety is weakly antigenic, as recited in claims 6-8, or wherein there is a plurality of antigen moieties, as recited in claim 5, or wherein said composition is formulated as a vaccine, as recited in claims 9-13. The limitations wherein the antigen is conjugated to the C-terminal end, as recited in claims 3-6, or on at least one end of the heavy and light chains, as recited in claim 4 of the instant application, would be encompassed by the claims of the '480 patent because one of ordinary skill in the art would be motivated to attach said antigen to the C terminal end, as this site is well known to artisans to attach conjugates to the C-terminus of proteins. Additionally, the limitations of claims 1 and 27 of the instant application that the antibody is bivalent having heavy and light chains would be encompassed by the antibody recitations of the '480 patent. Claim 11 of the instant application is included because one of ordinary skill in the art would recognize that an antigenic epitope requires more than 5 amino acid residues, therefore, the limitation would be encompassed by the limitations of claim 5 of the '480 patent.

40. Claims 1-11, 27 and 28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,194,254.

41. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conjugate antibody molecule, specific for an antigen presenting cell surface structure, which express major histocompatability complex antigens class I and II , as recited in claim 2 of the instant application, comprising an antigen, as recited in claims 1 and 27, or wherein the antigen moiety is weakly antigenic, as recited in claim 7,

or wherein there is a plurality of antigen moieties, as recited in claims 8-10, or wherein said composition is formulated as a vaccine, as recited in claim 28, is not patentably distinct over the antibody conjugate recited in the '254 patent. The '254 patent recites an antibody conjugate molecule, specific for an antigen presenting cell surface structure (antigen presenting cells comprise dendritic cells, as recited in claim 2 of the instant application), comprising an antigen, as recited in claim 1, or wherein the antigen moiety is weakly antigenic, as recited in claims 6 and 7, or wherein there is a plurality of antigen moieties, as recited in claim 2, or wherein said composition is formulated as a vaccine, as recited in claims 8-12. The limitations wherein the antigen is conjugated to the C-terminal end, as recited in claims 3-6, or on at least one end of the heavy and light chains, as recited in claim 4 of the instant application, would be encompassed by the claims of the '480 patent because one of ordinary skill in the art would be motivated to attach said antigen to the C terminal end, as this site is well known to artisans to attach conjugates to the C-terminus of proteins. Additionally, the limitations of claims 1 and 27 of the instant application that the antibody is bivalent having heavy and light chains would be encompassed by the antibody recitations of the '254 patent. Claim 11 of the instant application is included because one of ordinary skill in the art would recognize that an antigenic epitope requires more than 5 amino acid residues, therefore, the limitation would be encompassed by the limitations of claim 7 of the '254 patent.

Conclusion

42. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 305-3014 or (703) 308-4242.

43. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mary Tung whose telephone number is (703)308-9344. The Examiner can normally be reached Tuesday through Friday from 8:30 am to 6:00 pm. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1640 receptionist whose telephone number is (703) 308-0196.

Mary Tung
April 7, 1999
Mary B. Tung, Ph.D.
Patent Examiner
Group 1640

David A. Saunders
DAVID SAUNDERS
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ART UNIT ~~182~~ 1644